

CLAIMS

1. A mutant pro-neurotrophin for use in intracellular processing of a corresponding growth factor having improved secretion efficiency as compared to a wild-type growth factor, wherein the wild-type pro-neurotrophin has an asparagine residue at a position 8 amino acids upstream from the site of cleavage for the mature growth factor, the mutant pro-neurotrophin comprising a polypeptide in which the wild-type asparagine residue is replaced by a basic residue.

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2. The mutant pro-neurotrophin according to Claim 1, wherein the basic residue is serine.

10 3. The mutant pro-neurotrophin according to Claim 1, wherein the corresponding growth factor is selected from the group consisting of neurotrophins NGF, NT-3 and BDNF.

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4. The mutant pro-neurotrophin according to Claim 1, wherein the polypeptide is a recombinant one, and the replacement of the wild-type asparagine is made by mutation of a polynucleotide encoding the wild-type pro-neurotrophin.

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5. A mutant pro-neurotrophin for use in intracellular processing of a corresponding growth factor having improved secretion efficiency as compared to a wild-type growth factor, wherein the wild-type pro-neurotrophin has an asparagine residue at a position 4 amino acids upstream from the site of cleavage for the mature growth factor, the mutant pro-neurotrophin comprising a polypeptide in which the wild-type asparagine residue is replaced by a basic residue.

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6. The mutant pro-neurotrophin according to Claim 5, wherein the basic residue is serine.

7. The mutant pro-neurotrophin according to Claim 5, wherein the corresponding neurotrophin is NT-4/5.

30 8. The mutant pro-neurotrophin according to Claim 5, wherein the polypeptide is a recombinant one, and the replacement of the wild-type asparagine is made by mutation of a polynucleotide encoding the wild-type pro-neurotrophin.

9. A mutant pro-neurotrophin precursor polypeptide selected from the group of polypeptides consisting of SEQ.ID.Nos. 1, 3, 5 and 7.

35 10. A mutant pro-neurotrophin comprising the precursor polypeptide of Claim 5 joined by a cleavage site to a corresponding mature growth factor.

11. A polynucleotide encoding a mutant pro-neurotrophin, wherein the polynucleotide differs in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 8 amino acids upstream from the site of

cleavage for the corresponding growth factor, with a substitution codon encoding a basic residue.

12. The polynucleotide according to Claim 7, wherein the substitution codon encodes serine.

13. The polynucleotide according to Claim 7, wherein the corresponding neurotrophin is
5 selected from the group consisting of NGF, NT-3 and BDNF.

14. The polynucleotide of SEQ.ID.No. 16.

15. A polynucleotide encoding a mutant pro-neurotrophin, wherein the polynucleotide differs
10 in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 4 amino acids upstream from the site of cleavage for the corresponding neurotrophin, with a substitution codon encoding a basic residue.

16. The polynucleotide according to Claim 15, wherein the substitution codon encodes serine.

17. The polynucleotide according to Claim 15, wherein the corresponding neurotrophin is
15 NT-4/5.

18. A recombinant expression vector containing the polynucleotide of any of Claims 11, 14 or
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19. A host cell containing the recombinant expression vector of of any of Claims 11, 14 or
15.

20. A pharmaceutical composition comprising the recombinant expression vector of of any of
Claims 11, 14 or 15.

21. A pharmaceutical composition comprising the host cell of any of Claims 11, 14 or 15.

22. A process for producing a mutant pro-neurotrophin for use in intracellular processing of a
25 corresponding growth factor having improved secretion efficiency as compared to wild-type growth factor, the process comprising (a) synthesis of the mutant pro-neurotrophin encoding polynucleotide, wherein the polynucleotide differs in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 8 amino acids upstream from the site of cleavage for the corresponding growth factor, with a substitution codon encoding a basic residue; and (b) causing the synthetic polynucleotide to express the pro-neurotrophin.

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23. The process according to Claim 22, wherein the polynucleotide of Claims 11 or 14 is produced by step (a).

24. A process for producing a mutant pro-neurotrophin for use in intracellular processing of a corresponding growth factor having improved secretion efficiency as compared to wild-type growth factor, the process comprising (a) synthesis of the mutant pro-neurotrophin encoding polynucleotide, wherein the polynucleotide differs in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 4 amino acids upstream from the site of cleavage for the corresponding growth factor, with a substitution codon encoding a basic residue; and (b) causing the synthetic polynucleotide to express the pro-neurotrophin.

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10 25. The process according to Claim 22, wherein the polynucleotide of Claim 15 is produced by step (a).